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BULLOUS DERMATITIS AND BULLOUS PEMPHIGOID.

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BULLAE may be observed in acute eczema. The lesions of bullous pemphigoid may remain in one area of the skin for a variable period of time before spreading to affect the classical sites, and may be associated with other morphological changes closely simulating and often indistinguishable from those seen in eczema and in various "erythemata".

In 1949, Gordon and Loewenthal suggested that some cases of chronic idiopathic eczema might be variants of dermatitis herpetiformis; this hypothesis was based mainly on clinical grounds. Jarrett (1957) has recently shown by histological examination of very early lesions in dermatitis herpetiformis that the blister may form in an intraepidermal position by acantholysis. In 1954, Hellier drew attention to the fact that some cases of pemphigus showed subepidermal bullae. The usual histological criteria should not be too rigidly applied in blistering diseases, as features of one kind of process may appear in a different clinical context.

I would like to record another variety of bullous eruption, seen most commonly in elderly patients. It usually affects the lower limbs and is associated with localised or widespread eczema. It presents the histological changes of bullous dermatitis in some instances and that of bullous pemphigoid in others. Six examples of this condition have been seen at St. John's Hospital for Diseases of the Skin during the last few years.

CASE REPORTS.

Case 1. A man aged 59. Retired police officer. When first seen in July 1956, he gave a history of having had hypostatic eczema and ulceration of the right leg for a year, the ulcer healing after some months of routine treatment. He had suffered

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from bilateral varicose veins of the legs for some years and a Trendelenberg operation was performed on the left side in 1947. Ten days prior to his first attendance he developed swelling and redness of the skin of the right lower leg followed by a vesicular eczematous reaction and bullae. The eczematous eruption had spread to the other leg and to the arms. He was admitted to hospital and remained under observation for a period of four months (July to November 1956) during which eczema persisted on the arms and legs and was most troublesome on the right lower leg. During the whole of this period, bullae of varied size continued to form on the right lower leg but also to a lesser degree on the other limbs, ceasing in the latter sites after a period of four weeks, despite the persistence of the eczema. Two months after admission,



FIG. 1.

an acute exacerbation occurred, with bulla formation on the right lower leg and dissemination to the hands. This resulted from wearing a Kleinert's leg protector over the right leg while having a bath. He was discharged from hospital in November 1956 with residual hypostatic eczema of the lower legs and has since been under regular observation as an out patient. Mild chronic eczema persisted on the right lower leg until June 1958, and the last episode of blister formation was in May 1958. When last seen in September 1958 there was only residual dryness and pigmentation of the skin. A biopsy was performed of one of the bullae five to six weeks after the start of the eruption. Microscopical examination showed that the epidermis had been stripped off the inflamed papillae and replaced by exudate; elsewhere the necrotic epidermis remained as the roof of the bulla. In addition there was oedema and an inflammatory infiltrate in the papillae and subpapillary corium (Fig. 1). Dr. H. Haber considered that this was compatible with the clinical diagnosis of bullous dermatitis.

Case 2. A man aged 64. Retired police officer. He was first seen in November 1956 and gave a history of having had what he thought were insect bites around the right ankle in July of the same year. A scaly itchy eruption developed gradually around this site and one week before his first attendance it spread to all four limbs. A clinical diagnosis of eczema was made. There was no obvious cause including signs of venous insufficiency. Two months later (January 1957), whilst still suffering from an eczematous eruption on all four limbs, he was first noticed to have developed bullae on both lower legs. He then stated that his original lesions in July 1956 had also been blisters of the same type. He continued to develop bullae from time to

time over a period of nine months in association with eczema of the lower legs. No fresh bullae developed in the last twelve months although the eczematous eruption continued to erupt in a mild form on the legs and arms. Although most bullae formed at the height of the eczematous reaction, a limited number continued to



FIG. 2.

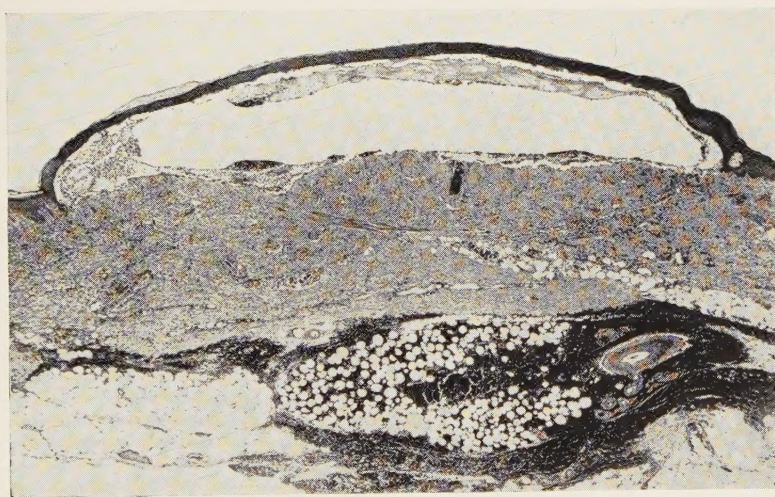


FIG. 3.

appear on the right lower leg when the eczema was quiescent. A biopsy of the skin of the lower leg in January 1957 showed the histological changes of eczema, viz., acanthosis and areas of spongiosis. In May of the same year a second biopsy, also from the lower leg, showed an intraepidermal bulla. This contained numerous polymorphonuclear leucocytes and there was a dermal infiltrate of round cells, some invading the epidermis, which in the base of the bulla showed patchy spongiosis (Fig. 2). Dr. H. Haber reported bullous pemphigoid.

Case 3. A woman aged 78. She was first seen in July 1958 with an eczematous eruption on the arms and legs. In one patch on the right lower leg there was a number of moderately large bullae mainly at the periphery of the eczematous plaque. She was noted to have classical discoid eczema on the trunk and limbs in August 1958 and this eczematous process continued to fluctuate in severity for six months when it virtually cleared (December 1958). Bullae remained confined to the affected area on the right lower leg and these blisters were also practically clear at her last visit. A biopsy of one of these blisters showed a subepidermal bulla with an inflammatory reaction in the cutis containing a large number of eosinophils (Fig. 3), changes identical with those found in bullous pemphigoid.

Case 4. A man aged 59. London Transport employee. When first seen in November 1956 he had an eruption of seven months' duration on both lower legs which was described as being erythematous, pigmented and excoriated. In addition, it was noted that he had a number of bullae of various sizes on the legs. He also had a mild papular eruption on the arms. He complained of itching which at times was severe. He was seen at monthly intervals during the next two years and was observed to have a recurrent eczematous eruption on the limbs and occasionally on the trunk, which never completely cleared. In addition, blisters formed repeatedly on both lower legs and over the dorsum of the feet. Even when the eczematous eruption on the legs was quiescent, the occasional blister formed. No blisters have appeared since December 1957. An irritating scaly erythematous eruption on the lower legs and papular eczema of the arms continued for a further six months. For the past five months, there has been no activity, either eczematous or bullous. In November 1957 a biopsy of the skin of the legs showed an acanthotic epidermis covered by a crust, with oedema of the upper cutis and newly formed vessels, compatible with chronic eczema. Cytological examination of a blister detected only inflammatory cells; no acantholytic cells were seen. He was treated initially with sulphapyridine with some improvement, but the blistering continued; dapsone (diamino-diphenylsulphone) was tried for a period of five weeks without obvious improvement.

Case 5. A man aged 60. Civil servant. He was first seen in January 1957 with a discoid eczematous eruption on the lower legs, associated with varicose veins but no other signs of venous insufficiency. In February 1957, the eczema spread to involve the arms, upper trunk and sacral region. He was also noticed to have flaccid bullae of various sizes on both lower legs. These continued to develop at intervals until March 1958. From April to August 1957 he was treated with systemic steroids with a maximum initial dose of 15 mg. of prednisone daily. There was improvement both in the eczematous eruption and the bullae although the occasional blister was seen from time to time on the legs. There was a slight relapse after the steroid therapy was discontinued but he remained reasonably controlled with topical therapy until February 1958. At that time he was admitted to hospital and the eruption cleared completely within a period of one month with routine local applications. A similar stay in hospital in March 1957 also resulted in complete remission. On both occasions relapse took place within a short period of discharge from hospital. On both occasions on admission to hospital he was noted to have eczema of legs, arms and trunk with bullae on the legs. A biopsy of a blister from the leg in April 1957 was unsatisfactory as there was complete separation of the epidermis and it showed only a denuded stratum papillare. Blister formation was last noted in March 1958 although a mild eczematous reaction persisted on the legs until his last visit as an out patient in December 1958. The eruption was unaffected by a month's course of dapsone, 50-100 mg. a day, at the end of 1957.

Case 6. A woman aged 41. She has suffered from recurrent attacks of eczema over the last twelve years. From July 1952 till October 1956 she attended the out patient department of St. John's Hospital with recurrent attacks of eczema of the scalp and ears, which was considered to be seborrhoeic. In October 1958 she was seen again after a lapse of two years with widespread eczema affecting the trunk and limbs of one month's duration. It was noted at that time that large bullae were present on the lower legs. She stated that these bullae had been recurring at intervals over the previous two years. A biopsy of one of these blisters (Fig. 4) showed the histological changes of vesiculo-bullous eczema. She was admitted to hospital and

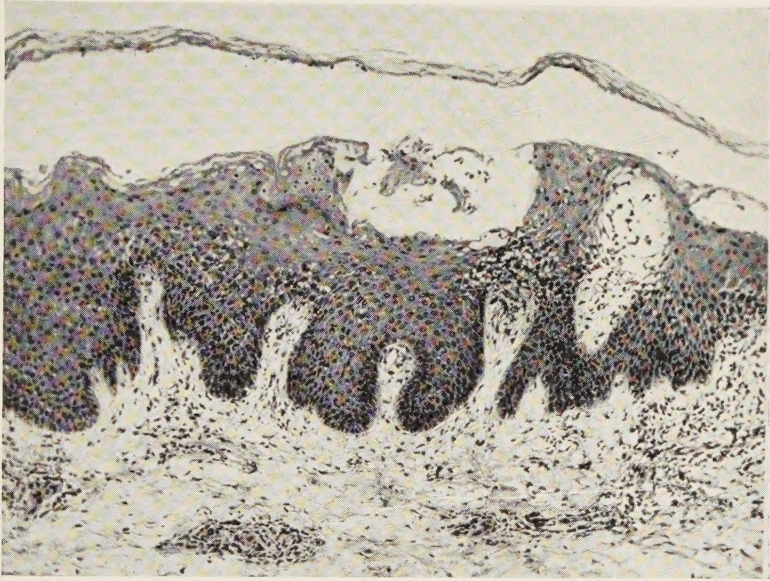


FIG. 4.

given a short course of prednisone and the eruption settled completely in six weeks. When last seen as an out patient in December 1958, the eczema was virtually clear and there had been no further blister formation.

TABLE I.—*Summary of Clinical and Histological Features.*

Case No.	Sex.	Age.	Sites affected.		Duration.		Histology.	Vari-cose veins.
			Eczema.	Bullae.	Eczema.	Bullae.		
1	M.	59	Arms and legs	Limbs (mainly right leg)	3 years	3 years	Eczema	Yes
2	M.	64	Arms and legs	Legs	2 years (still present)	1 year	1. Eczema 2. Pemphigoid	No
3	F.	78	Trunk and limbs	Right leg	6 months (still present)	6 months	Pemphigoid	No
4	M.	59	Trunk and limbs	Legs	18 months	1 year	Not diagnostic	No
5	M.	60	Trunk and limbs	Legs	2 years	1 year	Not diagnostic	Yes
6	F.	41	Trunk and limbs	Legs	4 months	4 months	Eczema	No

DISCUSSION.

In each of these cases the main morphological changes were those of eczema. The reaction usually started on the legs with a variable degree of secondary spread to the arms and trunk. In most of the patients the eczema was worse on the lower limbs. All were elderly with one exception (Case 6). Uncomplicated varicosity of the veins was present in one case and long standing varicosity with venous insufficiency and ulceration in another (Cases 1 and 5). In half the cases, the eczema persisted for a period of six to twelve months after bullae had ceased (Cases 2, 4 and 5). In most instances the degree of bulla formation was greatest when the eczematous reaction was at its height. It was interesting, however, that blisters in small numbers continued to appear in Cases 1 and 2 at times when the eczema was clear or minimal. In Case 2, in which a mild eczematous reaction still persists on the legs one year after the appearance of the last blister, the histology at one time was that of eczema and at another that of pemphigoid. In Case 3 in which the eczema was at one period widespread over the trunk and limbs, the histology of the blister was that usually seen in bullous pemphigoid and at all times the formation of blisters was confined to the skin on the right lower leg.

It is now well recognised that in bullous pemphigoid there may be areas of the skin with morphological changes simulating and often identical with those seen in eczema in addition to the classical blister formation. There may also be a background eruption resembling that seen in the "erythemata". Most of the clinical evidence in the six cases reported here is in favour of the disease being eczematous in type with additional bullae. They draw attention however to the fact that there may be clinical and histological findings in eczema identical to those which one might find in bullous pemphigoid. The skin is limited in its morphological and histological patterns of reaction. It would therefore not be right to try to associate the two conditions of bullous dermatitis and bullous pemphigoid.

SUMMARY.

Attention is drawn to a type of bullous eczema, usually affecting the legs of elderly patients with the histological changes either of eczema or of bullous pemphigoid. Six examples of this condition are reported.

I should like to thank the Consultant Staff of St. John's Hospital for permission to report these cases.

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GRENZ-RAY TREATMENT OF FAMILIAL BENIGN CHRONIC PEMPHIGUS

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NUMEROUS treatments for familial benign chronic pemphigus have been described. These have met with various degrees of success and there is still no specific therapy for this condition. This paper is an account of six cases treated with Grenz rays.

CLINICAL AND PATHOLOGICAL FEATURES.

Hailey and Hailey (1939) established the disease as a clinical entity under its present name. Their diagnostic criteria have made its recognition relatively easy. It begins in early adult life, affects both men and women and is frequently familial. The chronic course is punctuated by remissions and exacerbations. The skin of the flexures is affected and hot weather and friction usually make the condition worse. The primary lesion is a small flaccid vesicle arising on normal skin. Rupture of the vesicles leads to the formation of denuded, moist, cracked areas, often covered by dried exudate and parakeratotic crusting. The lesions are frequently misdiagnosed as intertrigo. Histologically, there are intraepidermal bullae with characteristically large numbers of acantholytic cells. The latter may also be found in smears of scrapings from affected areas and this technique is therefore useful in confirming the diagnosis in a clinically doubtful or suggestive case.

It was originally considered that familial benign chronic pemphigus was a vesicular (wet) variant of Darier's disease, but according to Pinkus and Epstein (1946) the two diseases may be differentiated clinically on the following grounds. (i) Familial benign chronic pemphigus is chronic and recurrent whereas Darier's disease is progressive. (ii) In spite of many years' duration, the changes of familial benign chronic pemphigus remain superficial and flat and the vegetating lesions, so characteristic of keratosis follicularis, never develop.

The basic histological difference between the two conditions is the lack of dyskeratotic features in familial benign chronic pemphigus (Jabłońska and Chorzelski, 1958).

TYPES OF THERAPY.

Hailey and Haily (1939) stated that "while simple wet dressings are palliative, apparently no treatment influences the course of the disease". However,

applications of various ointments, including antibiotics and steroids, often lead to temporary improvement.

Numerous systemic treatments have been advocated. Large doses of vitamin A had a considerable vogue (Fraser, 1942; Pinkus and Epstein, 1946; Ellis, 1950; Zoon *et al.*, 1951; Ingram and Collins, 1954), largely from the belief that familial benign chronic pemphigus was a variant of Darier's disease and could be treated similarly. Other vitamins (Schwarz, 1954), autogenous vaccines (Hailey and Hailey, 1939; Salsberg, 1950), chemotherapeutic agents and antibiotics have been tried but without consistent success (Carpenter, 1948; Norrlind and Blumenthal, 1949; Gougerot, 1950; Salsberg, 1950; Schwarz, 1954). Administration of steroids, both ACTH and cortisone (Zoon *et al.*, 1951; Korossy, 1956) produced temporary improvement.

Various irradiations, including Thorium X, superficial X-rays (Sutton, 1949) and Grenz rays (Ayres and Anderson, 1939; Rein, 1941; Ingram and Collins, 1954) have been reported to be effective. Fractional X-ray therapy of the affected region usually results in temporary improvement but the main disadvantage of short X-rays is that the total dose must be carefully controlled if serious sequelae are to be avoided. Their use is therefore not recommended for the management of a chronic disease such as this. It is suggested that the use of long-wave X-rays (Grenz rays) is a logical solution of the problem.

ADVANTAGES OF GRENZ-RAY THERAPY.

(i) *The superficial nature of the dermatosis.*—Although Grenz rays do not penetrate the skin more than 1 to 2 mm., this is sufficient to reach the site of the lesion.

(ii) *The regions affected.*—The relative incidence of affected sites is given by Korossy (1956) as neck 39%, flexures 27.4%, trunk 17.1%, extremities 9.3%, head 7.2%. In addition, the skin of the external genitalia (especially the scrotum) is often involved. According to Bucky and Combes (1954), the flexor surfaces of the extremities, the eyelids, ears, scrotum and the anterior aspect of the neck react to lower doses of Grenz rays than the skin of the other parts of the body, possibly because of the thinness of the corneous layer. It is important to bear this in mind when the affected skin covers structures that are particularly susceptible to X-irradiation, such as the testes.

(iii) *The chronicity of the condition.*—In general, this disease begins early in adult life and persists for several decades, varying in severity. It would appear that even repeated doses of Grenz rays do not lead to any serious sequelae. There is no record of keratosis, ulcer, epithelioma or leukaemia following Grenz-ray treatment and although pigmentation, superficial atrophy and telangiectasia are seen, sclerosis, permanent dryness, permanent epilation,

wrinkling and other sequelae of intermediate depth damage have not been found (Ryan, 1942). According to Bucky and Combes (1954) doses of 20,000 r or more of Grenz rays may be given over a period of years with impunity.

METHOD OF TREATMENT USED IN PRESENT SERIES.

A standard type of low voltage X-ray machine was used at 10 kV. When ever possible, symmetrical lesions were first selected for treatment. To outward appearances, both sides were treated similarly, but unknown to the patient, one of the affected regions was protected by a lead-rubber screen and this side acted as a control. After the efficacy of Grenz rays for a given area had been established, the remaining lesions were treated. Two dosage schemes were employed. Some lesions were treated with a single dose of 400 r. Others were treated with 200 r or 300 r on three successive occasions at weekly intervals.

TABLE I.—*Summary of Clinical Findings.*

Case No.	Sex.	Age.	Sites affected	Duration in years.	Family history.
1	F.	48	Axillae, groins, neck	30	Positive
2	"	47	Axillae, groins, neck, anal fold	11	"
3	M	36	Groins, axillae, back of neck	3	Negative
4	"	41	Elbow flexures, neck, left axilla	2	Positive
5	"	38	Groins, axillae, neck, scrotum	6	Negative
6	"	54	Ditto	30	Positive

CASE REPORTS.

Case 1.—A married woman aged 48. The condition began in both axillae at the age of 18 years with "abscesses" and continued to affect the axillae, groins and at times, the sides of the neck. It has varied in severity and there have been occasional spontaneous remissions. A brother and sister of the patient are subject to a similar skin condition. When the patient was seen at the beginning of September 1957, both axillae showed moist intertriginous lesions, the right side being more severely affected than the left. The groins were only slightly involved. Cytological examination showed the presence of many acantholytic cells. In September 1957, Grenz-ray therapy was started in the right axilla. This consisted of 200 r weekly for three weeks. The left axilla was similarly "treated", protected by a lead-rubber screen and acted as a control. Within three weeks, there was striking improvement in the condition of the right axilla, whereas the left side continued to show moist intertriginous lesions. At the end of October 1957, the left axilla and both groins were similarly treated with three doses of Grenz rays, 300 r at weekly intervals. These treated sites cleared up. The condition reappeared in the right axilla at the end of January 1958, i.e. five months after treatment with Grenz rays and a second course totalling 600 r had to be given. When the patient was seen at the end of March 1958, all the previously affected sites showed only minimal involvement.

Case 2.—A single woman aged 47. A weeping dermatosis of the axillae, groins, neck and anal fold began in 1947, when she was 36. The condition had always been worse during the summer months. In 1954, a clinical diagnosis of Hailey-Hailey disease was made and confirmatory cytology showed the presence of numerous acantholytic cells. The patient's father and grandfather both suffered from a similar condition. A number of topical applications was tried without much success before treatment with Grenz rays was started. The former included aureomycin ointment, potassium permanganate soaks, Lassar's paste and 2½% hydrocortisone ointment. However, a course of conventional X-rays (75 r, 60 kV on two occasions, 50 r, 60 kV, one dose) given in 1954 to the right groin and left axilla produced temporary remission. Grenz-ray therapy was started in March 1957. Both axillae were given three doses of 200 r at weekly intervals, the left side being screened and acting as control. In May 1957, the axillae showed a striking contrast: the right side was dry and healed, the left was moist and showed no improvement. Subsequently, both groins were treated with a similar dose and in the same way. Again the treated side responded. Activity on the side and back of the neck was effectively suppressed by a single dose of 400 r. The other affected areas were then given Grenz rays and by July 1957 the condition of her skin was excellent. Two of the sites first treated in March 1957 began to show a little activity for the first time six months later and a second course of Grenz rays was prescribed. Her disease was satisfactorily controlled for a period of sixteen months by Grenz-ray treatment.

Case 3.—A man aged 36. When this patient was first seen in January 1955, he had had a rash for nine months, affecting the left groin and the left axilla, later spreading to the right groin and axilla and to the back of the neck. A biopsy confirmed the clinical diagnosis of familial benign chronic pemphigus. The family history was negative. There was no appreciable improvement with topical hydrocortisone or a combination of hydrocortisone and neomycin. Slight improvement was noted following therapy with conventional X-rays in 1955 (three exposures of 75 r, 60 kV). When the patient was seen again in June 1957, both axillae were clear. The left groin, however, was moist and cracked, showing the typical features of familial benign chronic pemphigus. Grenz-ray treatment was given, consisting of 300 r on three occasions at weekly intervals. At the end of this period the skin of the left groin was dry and healed. When the patient was seen with marked "intertriginous" changes of the right groin in August 1958, it was noted that the left groin had remained healed.

Case 4.—A man aged 41. This patient gave a two years' history of a weeping, blistering eruption affecting the elbow flexures. On a previous occasion, he had had a rash on the neck. The condition was worse in the summer months and apparently was irritated by the application of plaster and ointments. A brother was similarly affected. Examination showed a plaque of recent blistering with residual crusts in the right antecubital fossa. There were only mild changes in the left elbow flexure. There was also an eroded patch in the left axilla. Cytology revealed the presence of acantholytic cells. Three exposures of Grenz rays, 200 r each, were given to the right elbow flexure in January 1958. In March 1958, the area was dry and healed, showing only some linear crusting at the periphery of the patch and a moderate degree of pigmentation of the treated skin. When he was seen again in August 1958, it was noted that he was clear except for a little soft scaling in the axilla.

Case 5.—A man aged 38. He was first seen in October 1952 with a 4 months' history of a rash affecting the groins, the axillae and neck. Later, the scrotum became involved. He was subject to yearly exacerbations and he insisted that the condition was worse in the winter months. There was no relevant family history.

In December 1956 the axillae and the groins were treated with superficial X-rays (three doses of 75 r, 30 kV). The axillae improved but the groins continued to be troublesome. By August 1957, the lesions in the groins were very much worse and Grenz rays, 300 r on three occasions at weekly intervals, were given to both groins, the left side being screened and acting as control. Marked improvement followed in the right groin. The skin of the left groin, however, continued to be moist and cracked and by the middle of November 1957, both axillae were similarly affected. The axillae and left groin were therefore treated with Grenz rays, 300 r thrice to each site. In February 1958 their condition was very good. The improvement was maintained and in June 1958, both axillae were healed, although a few cracks were noted in the groins.

Case 6.—A man aged 54. He had been troubled for 30 years by a rash which affected his groins and scrotum and occasionally the axillae and neck. A sister suffered from a similar condition. The diagnosis of familial benign chronic pemphigus was confirmed by cytological examination. In October 1957, both groins were treated with Grenz rays, three doses of 300 r, the right groin acting as control. The left side improved rapidly. In February 1958 the right groin was also successfully treated with a total of 900 r. In May 1958, the weeping and cracked skin of the scrotum was treated with Grenz rays, three doses of 200 r. When the patient was seen in June 1958, the scrotum showed very little improvement, but the groins remained satisfactory. The clinical findings and results of treatment are summarized in Table I and details of treatment in Table II.

TABLE II.—*Summary of Radiotherapy.**

Case No.	Site.	Area treated.	F.S.D. (cm.).	KV.	Dose (r)	Interval (weeks)	Number of doses.	Total dose (r).	Remission (months).
1	R. axilla	Circle 14 cm. diameter	30	10	200	1	3	600	5
	Ditto		30	10	200	1	3	600	2 +
	L. axilla		screened as control						0
		Circle 14 cm. diameter	30	10	300	1	3	900	6 +
	Groins	" " "	30	10	300	1	3	900	6 +
	R. axilla	Circle 11 cm. "	20	10	200	1	3	600	6
		" " "	30	10	300	1	3	900	8 +
	L. axilla		screened as control						0
		Circle 11 cm. diameter	20	10	200	1	3	600	6
		" " "	30	10	300	1	3	900	8 +
2	R. groin	" " "	20	10	200	1	3	600	6
		" " "	30	10	300	1	3	900	9
	L. groin	" " "	20	10	200	1	3	600	10
		" " "	30	10	200	1	2	400	4
	Anal fold	Square 7 cm. side	30	10	200	1	3	600	12
	R. side of neck	Circle 5 cm. diameter	10	10	400	0	1	400	11
	Back of neck	Circle 8 cm. "	20	10	400	0	1	400	9
	Thighs	Circle 14 cm. "	20	10	200	1	2	400	4 +
	L. groin	Circle 11 cm. "	20	10	300	1	3	900	14 +
	R. groin		screened as control						0
3	R. elbow	Circle 6 cm. diameter	10	10	200	1	3	600	8 +
	R. groin	Circle 11 cm. "	20	10	300	1	3	900	10
	L. groin		screened as control						0
		Circle 11 cm. diameter	20	10	300	1	3	900	7
	Scrotum	Circle 8 cm. "	20	10	300	1	3	900	8 +
	Axillae	Circle 14 cm. "	20	10	300	1	3	900	8 +
	L. groin	Square 7 cm. side	30	10	300	1	3	900	8 +
	R. groin		screened as control						0
		Square 7 cm. side	30	10	300	1	3	900	4 +
	Scrotum	" " "	30	10	200	1	3	600	0

* Inherent filtration equivalent to 1 mm. Al.

DISCUSSION.

It is possible that familial benign chronic pemphigus is a developmental condition and therefore incurable. Nevertheless, it seems that a reasonable period of control of the disease can be achieved by Grenz-ray therapy which has the advantage that it does not produce serious sequelae even after repeated administration to the same site.

In the six cases described, treatment with Grenz rays was effective for at least several months. The period of follow-up ranged from 8 to 16 months and the remissions which followed treatment lasted from 4 to 14 months. The length of remission is consistently greater than that obtained with any other single measure. The divided-dose scheme appeared to give better results than the single-dose method. There does not seem to be much difference between the results obtained by the use of three doses of 200 r or three doses of 300 r at weekly intervals, although the latter on occasion proved more effective.

SUMMARY.

Six cases of familial benign chronic pemphigus treated with Grenz rays are reported and the relevant literature is reviewed.

It has been found that Grenz-ray therapy produces consistently longer periods of improvement than any other treatment and it has other advantages.

I am grateful to the Physicians of St. John's Hospital for Diseases of the Skin for permission to treat their patients.

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SUBCORNEAL PUSTULAR DERMATOSIS OF THE SOLES.

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WE wish to report a case of persistent vesiculo-pustular eruption of the soles in which the lesions were peculiar in that they showed a pus level below clear fluid. The appearance was distinct from that of pustular psoriasis or of pustular dysidrosis.

CASE REPORT.

A man aged 58. A blistering eruption had been present on the feet for over two years. There did not seem to have been any itching in relation to these blisters. Over the same time the finger and toe nails had become distorted and there were

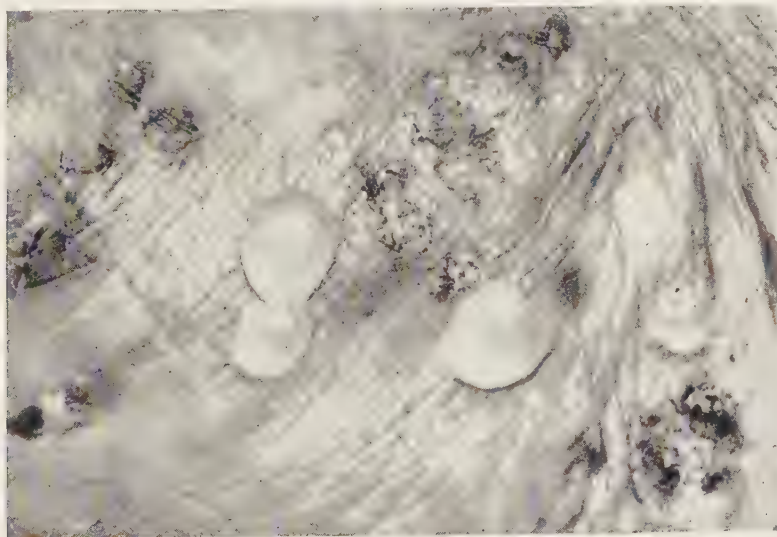


FIG. 1.

multiple paronychiae. The skin of the legs had been damaged by scalding two and a half years ago and some dermatitis had persisted. He had had psoriasis since he was six years old and one of his sisters also had psoriasis. He gave a confused history: he had advanced arteriosclerosis.

He was found to have plaques of psoriasis on the elbows and knees and lichenified dermatitis on the shins. There was intertrigo in the genitocrural folds. Finger and toe nails showed dystrophy and thickening and there was severe paronychia. The soles of the feet were covered with flaccid vesiculo-pustules of which the larger were about 1 cm. in diameter. The pus was to be seen as a sediment in the dependent part of each blister in the manner of hypopyon (Fig. 1). With treatment in hospital the

skin lesions cleared up except for the vesiculo-pustules of the soles. These continued to appear steadily during five months in hospital. There was no response to rest in bed, local applications, superficial X-rays or diaminodiphenyl sulphone, or to suppression of sweating by probanthine.

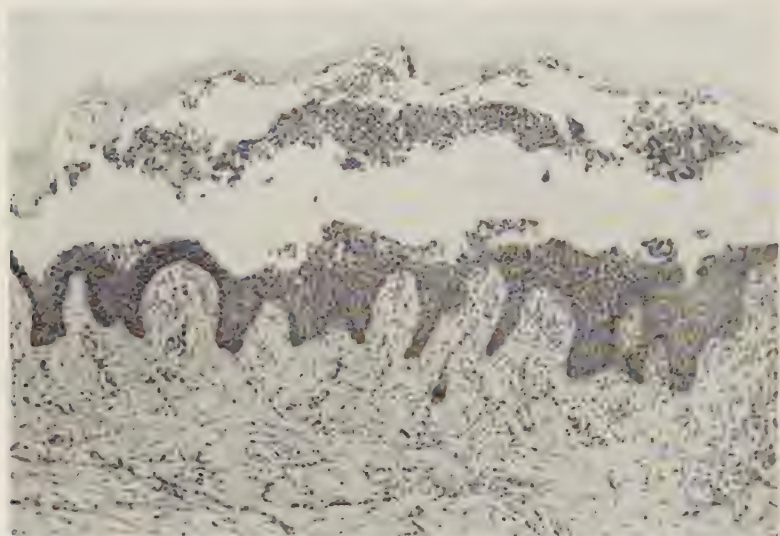


FIG. 2.

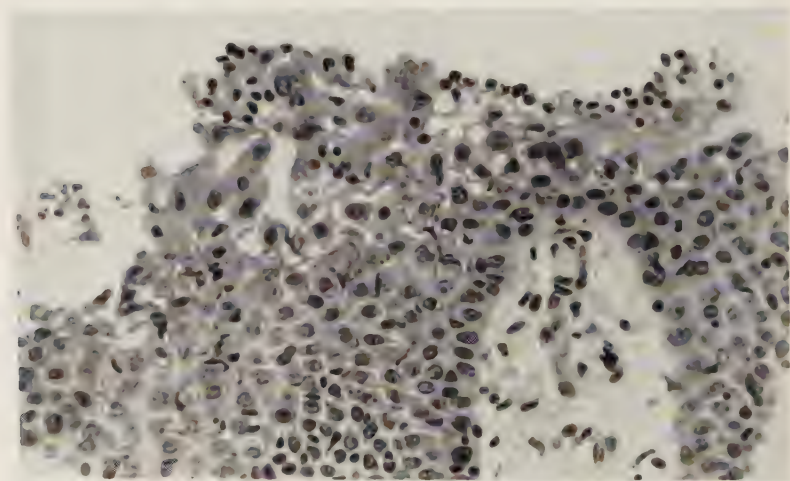


FIG. 3.

Repeated examinations of scales and blister tops from the feet and nails showed no evidence of fungus infection on microscopy and culture. Bacteriological cultures from the vesiculo-pustules on several occasions were sterile. The pH of the blister fluid was the same as that of serum. A vesiculo-pustule from the sole was removed for histological examination. The epidermis showed acanthosis and immigration of

a few inflammatory cells. The main feature was the presence of a subcorneal bulla filled with neutrophils (Fig. 2). The roof of the bulla was intact and consisted of the stratum corneum. The base of the bulla appeared to have undergone acantholysis (Fig. 3). A few cells were swollen and had lost their prickles. One or two acantholytic cells were seen intermingled with neutrophils lying within the bulla. The upper corium exhibited an inflammatory reaction which was mild considering the heavy accumulation of polymorphs under the stratum corneum.

DISCUSSION.

The unusual feature of this case was the persistence of large vesiculo-pustules on the soles over many months even though the patient was at rest in bed, and even though the other lesions (psoriasis and lichenified eczema) had been cleared. These persistently recurrent blisters on the feet always showed a sediment of pus with a visible level between it and the clear fluid above. In this respect individual lesions resembled the subcorneal pustular dermatosis of Sneddon and Wilkinson (1956), but it is unknown for such lesions to be confined to the feet; in fact the palms and soles are spared in that condition. Hellier (1956) reported a case of this subcorneal pustular dermatosis in which the characteristic lesions appeared on the trunk, whilst small pustules of the kind sometimes called "pustular bacteride" had been present on the soles and palms for six years. Apparently the pustules on the soles were not examined histologically and from the description of the case, it is uncertain that they had any relation to the subcorneal pustular dermatosis on the trunk.

In our patient, the histological appearance of the vesiculo-pustule was different from that which is seen in pustular psoriasis or so-called "pustular bacteride". There was nothing to suggest psoriasis and none of the "spongiosis" described by Kogoj (1927) as characteristic of pustular psoriasis or pustular bacteride. Our section showed remarkably little inflammation in the dermis and it would appear that the polymorph neutrophils had gravitated slowly into the region of the granular layer, where some acantholysis was to be seen. Bullous impetigo was ruled out bacteriologically and pemphigus foliaceus was excluded on clinical grounds. We are left then with an eruption on the soles, with individual lesions clinically and histologically resembling the subcorneal pustular dermatosis of Sneddon and Wilkinson.

We wish to thank Mr. R. J. Lunnion of the Institute of Dermatology for the photographs.

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A FATAL CASE OF ERYTHEMA MULTIFORME FOLLOWING DEEP X-RAY THERAPY.

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COMPARATIVELY few cases of generalized skin reactions following deep X-ray therapy have been reported. Probably the first published record of such a reaction following moderately severe local X-ray dermatitis is that of Holzknecht (1903), a Viennese radiologist, who drew attention to the condition. Sporadic reports on this syndrome have appeared in various journals since then (Schreiner, 1924; Epstein, 1926; Pardo-Castello, 1936; Enfield, 1937; Kautzky, 1937; Loewe and Camiel, 1940; Castigliano, 1941; Maccagno, 1941; Arnold, 1949; Sulzberger and Baer, 1949; Mazzini, 1953.) The only reference in the British dermatological literature is by Goldsmith and Hellier (1954), who report a case of very severe and widespread erythema multiforme with bullae and intense itching, after irradiation of the spine for secondary carcinoma. In 1952, Davis and Pack reviewed the literature and collected thirty-one cases, to which they added five of their own.

The syndrome has a characteristic history, physical signs and laboratory features. A generalized rash appears two to twenty-one days after commencing deep X-ray therapy. The rash may be erythematous, papular, lichenoid, vesicular, bullous, scarlatiniform, purpuric, morbilliform or exfoliative. It is frequently associated with hyperpyrexia and other constitutional symptoms including nausea and vomiting, weakness, prostration, joint pains, tachycardia and pruritus. The constitutional symptoms may persist as long as a month.

Nowadays, deep X-ray therapy is employed mainly for carcinoma either alone or following surgical resection, but the primary disease does not seem to play a major part in the syndrome. Holzknecht (1903) reported five cases in patients whom he had treated for facial hirsutes, psoriasis or favus. Kautzky (1937) described two cases in patients given deep X-ray therapy for hyperthyroidism and haemolytic jaundice respectively. The only fatal case, reported by Epstein (1926) was one of generalized purpura following deep X-ray therapy for cancer of the uterus.

CASE REPORT.

The patient was an unmarried woman aged 65 years, who was first seen by a surgeon with a diffuse scirrhous carcinoma of the left breast, showing retraction of the nipple and overlying skin. Lymph nodes were palpable in the left axilla but were not fixed.

There was no spinal tenderness. The patient was admitted to a surgical ward and apart from the condition of the left breast and a blood pressure of 210/120 mm. Hg., there were no abnormalities on examination. A radiograph of the chest showed normal lung fields. A simple mastectomy was performed and convalescence was uneventful. Histological examination of the breast confirmed the diagnosis of scirrhus carcinoma.

About eight weeks after the surgical operation, she began X-ray therapy to the left axilla and supraclavicular region. Treatment was spread over eighteen days, using opposed fields, 25 by 12.5 cm. anteriorly, 15 by 10 cm. posteriorly, giving a central



FIG. 1.

dose of 3546r and a maximum dose of 4500r. Filtration triple Thoraeus, H.V.L. 3.5 mm. Cu. The chest wall was also treated by opposed glancing fields 15 by 10 cm. separated by 16 cm. with a central dose of 3750r and a maximum dose of 4274r. Filtration single Thoraeus, H.V.L. 2.5 mm. Cu. The patient was then sent home with instructions to dress the expected area of local reaction with calamine lotion, or with zinc and castor oil ointment if the skin blistered.

She was admitted to the skin ward two weeks after the last X-ray treatment with a generalized eruption which had started approximately eight days after the final dose of X-rays. She also gave a history of nose bleeds and slight nausea but no vomiting. She had not taken any drug or used any local treatment other than calamine lotion. Examination showed an obese woman whose face, trunk and limbs were covered with a erythemato-macular rash, with a denuded area around a surgical scar on the left side of the chest, extending over the clavicular region (Fig. 1). The face was oedematous and the eyelids, anterior nares and lips showed crusted haemorrhagic lesions. There were no lesions in the mouth, pharynx or vagina. Her temperature was 103° F., pulse 120 and blood pressure 132/80 mm. Hg. The chest, cardio-

vascular and central nervous systems and abdomen were normal. A clinical diagnosis of erythema multiforme was made. The histology of a biopsy specimen of skin, taken the following day, was consistent with the diagnosis, although an unusually large number of chronic inflammatory cells was noted in the subepidermal bullae and in the dermis itself (Fig. 2). Hb. 78%, W.B.C. 4,100 per cu.mm., no abnormalities in

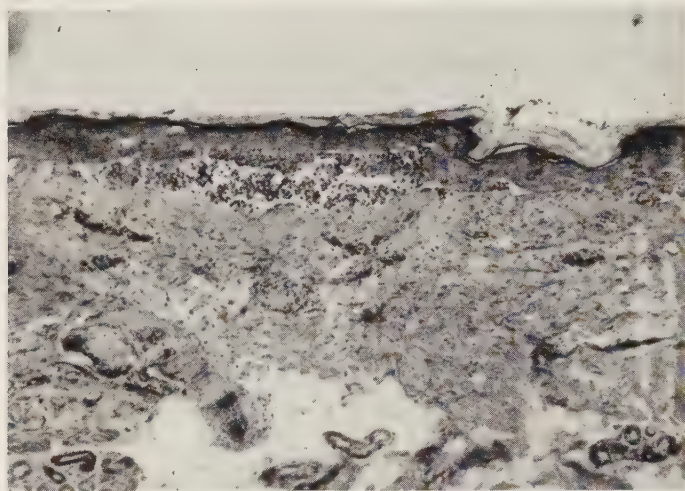


FIG. 2.

the white blood cell series. No eosinophilia and normal platelets. Serum electrolytes and blood urea normal. A swab from the blistered area on the left side of the chest showed no organisms in a smear and culture was negative.

Treatment was commenced on admission with diphenhydramine hydrochloride (Benadryl) 50 mg. four times a day and sodium amytal 3 grains at night. Two days after admission, the pulse and temperature remaining at the same level she was given tetracycline (Achromycin) 250 mg. six hourly. Her condition remained stationary for the next two days. The skin started to shed without any real blister formation and her general condition deteriorated. She was then given methylprednisolone (Medrone) 8 mg. four times a day. The following day she was transfused with 500 ml. of 5% dextrose in water and 5% dextrose in normal saline alternately, as she had developed signs of dehydration. As there was still no improvement in her general condition, the antibiotic was changed to sodium penicillin, streptomycin sulphate and dihydrostreptomycin sulphate (Crystamycin) and the antihistamine to chlorpheniramine maleate (Piriton). At this stage, fine crepitations were audible at both lung bases. Next morning, seven days after admission, the patient died in coma.

Autopsy.—An area of haemorrhagic ulceration was present just below the level of the tracheal bifurcation. The trachea and main bronchi contained copious viscid muco-purulent secretion. Metastatic carcinomatous deposits were noted in both lungs and in the hilar lymph nodes on the right.

The adrenals showed central autolysis and patchy depletion of cortical fat.

The kidneys were normal in size and showed slightly granular surfaces from which the capsule stripped freely; the cut surfaces showed normal cortical and medullary markings.

The significant histological report was as follows. “*Lungs*: Histological examination reveals congestion, oedema and subpleural deposit of anaplastic carcinoma,

which is also seen in perivascular lymphatic vessels in the lung substance. Occasional intra-alveolar corpora amylacea are noted. Several elastic pulmonary arteries show notable irregular intimal fibrous thickening, either nodular or completely encircling the lumen and some of these lesions contain fibrin, red blood cells and numerous fibroblasts, the appearances being those of organizing thrombus. There is no inflammatory reaction or fibrinoid necrosis in the media of these arteries but in some there is evidence of damage to elastic fibres and it seems likely that the lesions are due to deep X-ray therapy. *Hilar lymph nodes* : The presence of anaplastic carcinoma is confirmed, showing a very scanty stroma and much necrosis. *Liver* : There is mild, irregularly distributed fatty change and conspicuous centrilobular liver cell necrosis. Focal chronic inflammatory-cell infiltration of portal tracts is present. *Kidneys* : There are mild nephrosclerotic changes but no other notable abnormalities. *Oesophagus* : The presence of ulceration is confirmed and it is associated with haemorrhage and vascular thrombosis in the mucosa. There is a notable cellular infiltrate consisting of chronic inflammatory and neutrophil polymorphonuclear leucocytes. Adjacent to the ulcerated area, foci of necrosis are seen in the epithelium with the formation of intra-epithelial vesicles, the appearances being similar to those seen in the skin. The precise significance of this oesophageal lesion is not clear but it seems likely that it is of the same nature as the dermatitis."

DISCUSSION.

It would seem that in the past there has been reluctance to accept radiation as the cause of this syndrome, due perhaps to the resemblance of the rash to a drug eruption. Indeed, it must be uncommon to find a patient who does not take some analgesic or hypnotic drug after radiotherapy. Unaware of the possibility of a post-irradiation generalized rash, one would almost certainly implicate some drug. Loewe and Camiel (1940) reported skin reactions following deep X-ray therapy in four patients all of whom had received barbiturates at some time, but showed conclusively that the barbiturates played no important rôle in the development of the skin lesions. They continued to administer barbiturates and the skin reactions involuted. Davis and Pack (1952) bravely repeated deep X-ray treatment with repetition of the generalized skin eruption in two of their cases. Schreiner (1924) and Maccagno (1941) had similar experiences. This would seem strong evidence in favour of irradiation as the precipitating agent in this syndrome.

Enfield (1937) and Davis and Pack (1952) believed that the toxic erythemata occurring as a complication of irradiation were due to the rapid destruction of radiosensitive tumour, so that in those cases which eventually recover, the benefit from deep X-ray therapy might be expected to be greater than in the majority who do not develop such exanthemata. This theory does not hold good in every case, as has been pointed out by Holzknecht (1903) and Kautzky (1937), who saw similar reactions in patients treated with irradiation for conditions other than tumours. It seems to be accepted that the generalized skin eruption results from absorption of the products of cellular degeneration, the common finding of eosinophilia pointing to breakdown of protein.

The majority of cases reviewed in the literature seemed to respond to anti-histamines and this was taken as evidence of an allergic basis for the reaction. It has been shown that deep X-ray therapy releases histamine from the tissues and this is thought to play a part in the mechanism of radiation sickness. Antihistamines might be expected to counteract this response, presumably without implying an "allergic" origin as the histamine release was not due to an immunological reaction.

Another possibility in scarlatiniform, morbilliform and erythema multiforme type reactions is that bacterial infection at the irradiated site produces a toxin which in turn causes a skin reaction. Various authors have gone into this question, and in all the reported cases the likelihood of this aetiology was eliminated. If tissue breakdown from X-rays can produce a cutaneous response, other conditions where tissue breakdown occurs should produce such responses in at least some cases. Wittels (1954) reviewed 317 children admitted to hospital because of burns; a scarlatiniform exanthem occurred in 38. He concluded from the available data and his own examinations that at least 29 of the 38 had a toxic exanthem and not, as had been thought previously, true scarlet fever.

SUMMARY.

A review is presented of the literature on generalized skin reactions following deep X-ray treatment.

A case of fatal erythema multiforme after irradiation is recorded.

There seems little doubt that tissue breakdown is an aetiological factor in the reaction.

I am grateful to Mr. J. F. Philip and Dr. E. F. Ridley for access to the patient's case records; to Dr. T. E. Anderson and Dr. A. Lyell for helpful criticism in the preparation of this paper and to Dr. P. V. Best who performed the autopsy.

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A MONOCHROMATOR.

AN APPARATUS FOR THE INVESTIGATION OF THE RESPONSES OF THE SKIN TO ULTRA-VIOLET, VISIBLE AND NEAR INFRA-RED RADIATION.

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ONE of the most important matters requiring investigation in the photo-dermatoses is the determination of action spectra, i.e., the identification of the wavelengths of "light" (ultra-violet, visible and infra-red radiation) that provoke changes in the skin. Such information would be useful for two reasons. First, it would enable the clinician to choose an effective absorbing or reflecting application for use on the skin, as the application must prevent the penetration of those wavelengths which specifically initiate symptoms. Second, knowledge of the action spectrum of a disease might lead to an understanding of its pathogenesis or even to identification of the photosensitising substance. This is because radiant energy is only "active" after absorption, so that if the active wavelengths are known, a search can be made among the substances which are known to absorb them.

To find an action spectrum, the skin must be irradiated with narrow wavebands of known energy. This can be done either with the aid of filters, or with a monochromator. With absorption filters, the width of a waveband is wide, with interference filters, somewhat narrower. However, much the narrowest wavebands may be obtained with a monochromator, which seems to be the instrument to choose.

Schaumann and Lindholm (1932) appear to have been the first to use such an apparatus in a clinical investigation, employing the 297, 302 and 313 m μ lines from a mercury arc spectrograph to investigate a case of solar dermatitis. More recently, Burckhardt (1947), Beal (1948) and Porter (1954) have made similar but more detailed observations with spectrographs to elicit reactions in cases of solar urticaria.

As far as we are aware, up to now all workers who have used some form of monochromator have chosen the mercury arc as a source of illumination. For physiological studies, such as that of the normal sunburn reaction, this arc has much to recommend it (Coblentz, Stair and Hogue, 1932; Rottier, 1953). However, a serious disadvantage of the mercury arc in clinical investi-

gations is that its emission is in bands and lines, relatively few being present in the longer wavelengths of the ultra-violet spectrum. To overcome this defect, it was decided to use a light source emitting a strong continuum, e.g. the carbon arc. In a monochromator with such a source, the wavebands emitted would of necessity not be "single" spectral lines such as those from the mercury arc; but this disadvantage would be more than compensated by a very much greater useful spectral range.

Some results with the instrument now to be described have already been given by Magnus and Porter (1959) in a case of solar urticaria and by Magnus, Porter and Rimington (1959) in a case of porphyria cutanea tarda.

DESIGN AND CONSTRUCTION OF THE MONOCHROMATOR.

The lay-out of the optical components is shown in Fig. 1. The source, *S*, initially a high intensity carbon arc, is now a German Osram high pressure xenon arc (XBO

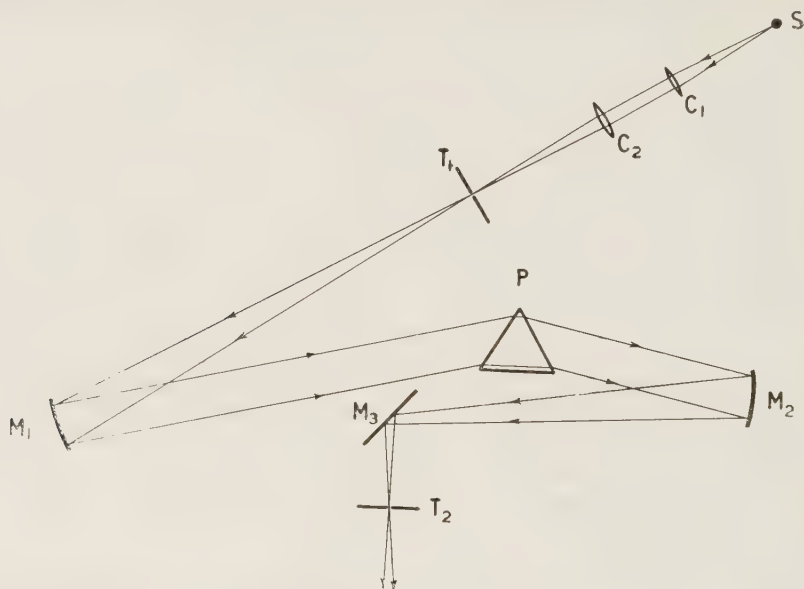


FIG. 1. Diagram of optical system of monochromator. *S* are source; *C*₁ and *C*₂ quartz condenser lenses; *M*₁ and *M*₂ parabolic mirrors; *P* water prism; *T*₁ and *T*₂ slits; *M*₃ plane mirror.

2001, quartz envelope), which has a very high luminance and radiates over an extended wavelength range. *C*₁ and *C*₂ are quartz condenser lenses which focus an image of *S* on the entrance slit, *T*₁. *C*₂ is adjustable to allow for the considerable change of focus when wave-lengths in the ultra-violet are used. *M*₁ and *M*₂ are surface aluminised parabolic mirrors of which *M*₁ collimates and reflects the light into the prism *P* and *M*₂ focuses it after dispersion in *P* to form a spectrum in the plane of the exit slit *T*₂, the beam having first been reflected in the plane aluminized mirror *M*₃. *T*₂, of robust construction to withstand patients' leaning against it, can be moved through the spectrum to change the wavelength of the emergent radiation. The position of *T*₂ is indicated on a calibrated wavelength scale.

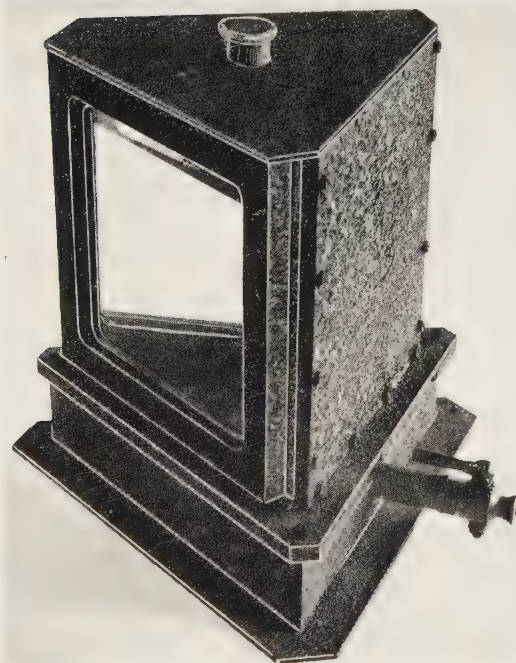


FIG. 2. Water prism housing.

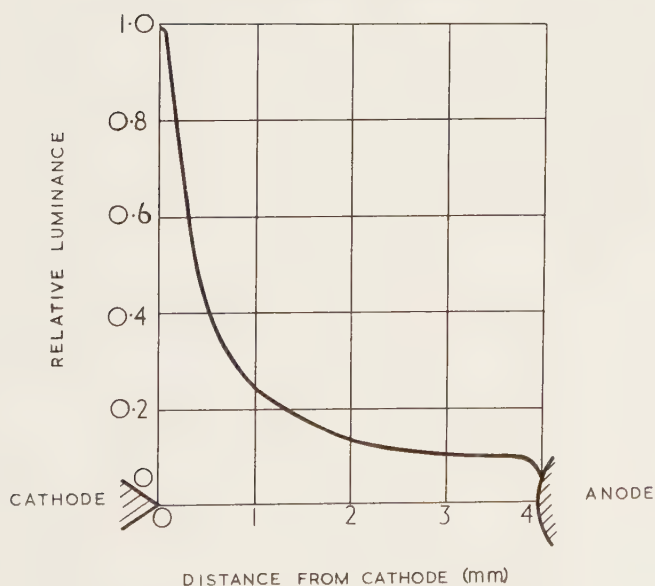


FIG. 3.—Graph to show variation of luminance along arc, data from Frühling, Münch and Richter (1955).

Distilled water was chosen as the material of the prism on account of its high transparency over the required wavelength range and its satisfactory dispersion characteristics, especially in the ultra-violet (Sawyer, 1951). Such a prism can also be constructed with a large aperture at moderate cost, so that the monochromator can be made highly efficient from the point of view of energy collection and transmission.

The construction of the prism is illustrated in Fig. 2. It consists of a 60° prism housing made of brass, fitted with quartz windows. Rubber gaskets between the windows and the housing are used to keep the prism watertight. A drainage pipe and tap are fitted to the base of the housing and a cap is provided in the top, so that the prism can be drained and refilled without removal from the instrument. The quartz windows, which were optically worked, are approximately 14 cm. square in size.

The other dimensions of the optical system are as follows: diameters of C_1 and C_2 6 and 8 cm., focal lengths 30 and 50 cm. respectively; parabolic mirrors 15 cm. diameter, 100 cm. focal length; distance of M_1 to first face of P 96 cm.; distance of second face of P to M_2 48 cm.; width of slits as normally used 2 mm.; size of M_3 , 20 cm. by 7 cm.; length of spectrum between 240 and 1000 $m\mu$, 7 cm. approximately; mean deviation produced by prism 27° . The components are mounted in optical bench fittings and attached to a wooden base. All except for the light source are housed in a dark room.

Periodic calibration of the wavelength scale showed that the stability of the system was satisfactory and no trouble was experienced from turbulence in the water prism or loss of clarity in the water once the initial debris and residual effects of soldering etc. had disappeared. The major problem with maintenance of the system has been with the aluminized mirrors, since their reflectivity diminishes rapidly in the London atmosphere. They have been re-aluminized from time to time and tests will be made shortly on a system of mangin mirrors designed by Professor B.K. Johnson (Johnson, 1934) to replace the parabolic mirrors. As the mangin mirrors are aluminized on the back surface, they will not be affected by the atmosphere.

Since the xenon lamp has been introduced, some difficulty has been experienced in securing uniform illumination along the lengths of the slits. A central band of higher luminance is present in the spectrum, evidently corresponding to the peak in luminance distribution across the source which occurs at the cathode as shown in Fig. 3. This is particularly noticeable in the ultra-violet wavelengths. Experiments at present being carried out normally use the central band of maximum luminance, the area of skin irradiated being 2 mm. by approximately 4 mm. It is not easy to see how this restriction can be avoided if full advantage is to be taken of the very high luminance of the xenon arc at its peak value.

The spectral purity required in the monochromator is of a lower order than that necessary in spectroscopy and it is legitimate to sacrifice purity in favour of light flux. For this reason, slit widths of 2 mm. have normally been used. No attempt has been made to keep the band widths constant throughout the spectrum and its variation with wavelength is shown in Fig. 4.

THE USE OF THE MONOCHROMATOR.

Before use on each occasion, the wavelength calibration of the instrument is checked and both before and after a set of exposures on the skin at one wavelength, measurement of energy output is made. Every few weeks, a test for the degree of scattered radiation is made.

Wavelength calibration.—This is done by placing a small medium pressure mercury arc at the first slit, T_1 , of the monochromator. The mercury arc spectrum formed at the second slit, T_2 , is seen on uranium glass. The spectral lines are identified in the ultra-violet by their characteristic grouping and relative intensity and in the visible

spectrum by their colour. The position of some of these lines is noted on the wavelength scale below the second slit. Checked in this way, the wavelength calibration has been found to alter extremely little from day to day.



FIG. 4.—Graph to show relation between width of waveband (slit widths 2 mm.) and wavelength.

Measurement of energy.—This is made with a Schwarz linear vacuum thermopile (Hilger, F.T.17) with quartz window and Tinsley galvanometer (type 4789) with sensitivity of 1360 mm. per micro-ampere at one meter scale distance. When measurements are made, the thermopile is screwed into the second slit, thus being in the same position as the skin during an exposure. So far only measurements of relative intensity have been made.

Owing to the great difference in the energy output from the light source over the spectrum, provision is made for altering the sensitivity of the galvanometer with a standard shunt circuit (potential divider), giving sensitivity ranges of approximately 1:1, 1:2, 1:20, 1:200 and 1:2,000. The ranges were calibrated more exactly by measuring the galvanometer deflection obtained when the thermopile was placed at various known distances from a tungsten lamp. Measurements of energy are made routinely before and after every set of exposures on the skin at each wavelength and have shown that the output remains steady for short exposures, but in exposures of over 20 minutes there may sometimes be a fall amounting to not more than 5%.

Test for scattered radiation.—Gradual deterioration of the surface of the mirrors leads to scattering, which causes "impurity" of the wavebands and a fall in energy. A measure of the amount of scattering is obtained by using the monochromator for estimating the transmission curves of a series of absorption filters, e.g. Chance OW1 and OX7, Corning 9701 and window glass. The curves found are then compared with transmission curves obtained by measurements in a Hilger "Uvispek" photoelectric spectrophotometer. If measurements with these filters indicate significant discrepancies, the mirrors are re-aluminized.

Method of use for testing the skin.—The subject sits with the skin of the back gently resting against the second slit of the monochromator. Exposures of light of graded duration are then given and the position of each test site is marked with ink immediately afterwards. Inspection is made for any effects immediately and at intervals, depending on the type of experiment or investigation. For measurements of the minimal erythema dose, a procedure similar to that of Rottier (1953) has been followed, viz. two-hourly inspections for about 16 hours and thereafter at longer intervals.

THE PERFORMANCE AND APPLICATION OF THE MONOCHROMATOR.

In normal adults with untanned skin, the exposure time required for a minimal erythema reaction on the skin of the back is 5 to 60 seconds at 250 m μ . and 1 to 5 seconds at 300 m μ . For some purposes, this intensity proves too high and has to be reduced by decreasing the current to the arc. At wavelengths approaching the visible range, exposures are somewhat longer, e.g. the duration required at 350 m μ . is of the order of 15 to 30 minutes. A more detailed account of results obtained from normal human skin and that of experimental animals will be given in a subsequent communication. Many applications for this instrument in biological research may be conceived apart from the investigation of human and animal photo-dermatoses. For instance, the monochromator would appear to be of suitable energy output for ultra-violet radiation carcinogenesis in the skin of experimental animals. It could also be used for determining the action spectra of substances which provoke photosensitivity, such as psoralen.

SUMMARY.

A monochromator is described which is designed for the irradiation of skin in the spectral range of approximately 250 to 1000 m μ . The source of illumination is a high pressure xenon arc and dispersion is effected by a water prism. Its method of use, performance and application are briefly given.

Thanks are due to Mr. A. E. Davis and Mr. W. E. Shand for the design and construction of the water prism, to Mr. M. Gadsden for making the parabolic mirrors, to the Ship Carbon Company for generously loaning apparatus and to the Medical Research Council and St. John's Hospital for Diseases of the Skin, London, for providing financial assistance towards buying equipment.

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THE VALUE OF TRIAMCINOLONE AND VITAMIN A IN THE TREATMENT OF PSORIASIS.

PRELIMINARY COMMUNICATION.

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THE histochemical and fluorescence changes in the skin of patients suffering from psoriasis have been investigated in this Department. The alterations produced by treatment with oral triamcinolone have also been studied and these have been compared with those obtained in the keratin of tail scales in mice and rats treated with triamcinolone. Clinical improvement in psoriatic cases treated with systemic triamcinolone has already been reported (Shelley *et al.*, 1958).

The tails of mice and rats have two types of keratin: that in the region of the follicular openings is formed with a granular layer and has been shown to be similar to human epidermal keratin. The epidermis of the tail scales, however, has no granular layer and its keratin closely resembles psoriatic parakeratotic keratin both in its fluorescence characteristics and histochemistry, but no nuclear chromatin remains (Jarrett *et al.*, 1959, in press). The chemical alterations produced in tail scale keratin by the local application of vitamin A have also been investigated by histochemical techniques and fluorescence microscopy.

Rats and mice were given parenteral triamcinolone. This caused marked thinning of the epidermis, with reduction of epidermal cell activity and the cytoplasmic content of ribonucleic acid. Similar changes occurred in psoriatic epidermis in patients under systemic treatment with this steroid and a granular layer was re-established quite rapidly. There was also a return of free glycogen and acid phosphatase activity in this region. In rodent tail scale, no granular layer was formed as a result of triamcinolone therapy and only slight changes occurred in the chemistry of the overlying keratin.

We repeated the experiments performed by Lawrence and Bern (1958) on the effects of local vitamin A on rodents' tails and confirmed that there was rapid formation of a granular layer in the tail scale epidermis together with greatly increased cellular activity and thickening of the epidermis. We thought that this stimulating action of vitamin A would aggravate psoriasis if vitamin A were applied to an area that was increasing in size: but if the condition were improving, then remission would be hastened by the use of a substance that effectively reformed a granular layer. As a result of our experiments, we concluded it would be worthwhile to investigate the clinical effects of local vitamin A

on psoriatic patients who had been previously treated with systemic triamcinolone. We also studied the effects of the combined application of a 0.1% triamcinolone cream containing 12,500 units of water solubilized vitamin A per gram.

CASE REPORT.

A man aged 61 years. Psoriasis for 15 years. Began on the right hip and gradually spread to involve large areas of the body. Many remissions and exacerbations, but he was completely clear on only one occasion 5 years ago. Two brothers have psoriasis and his daughter is also affected.

He was admitted to University College Hospital because of a recent severe exacerbation of psoriasis and was treated with local applications for 14 days with no improve-



FIG. 1.—The patient has been treated with Ledercort, 4 mg. b.d. for 11 days. The lesion on the upper arm has been treated for three days (six applications) with 0.1% Ledercort cream containing 12,500 units of vitamin A per gram. The lower lesion has been treated with ung. emulsificans aquos. (six applications) for three days.

ment. All local treatment was then stopped and he was given 4 mg. of Ledercort (triamcinolone) twice daily by mouth. After 8 days the lesions were less red, but they had not decreased in size.

One patch on the upper arm and another on the right thigh were then treated with Ledercort cream (0.1%) to which water solubilized vitamin A had been added in a concentration of 12,500 units per gram. After six applications in 72 hours these areas had almost cleared compared with the other lesions that had been treated with

ung. emulsificans aquos. (Fig. 1). The internal dose of Ledercort was not changed. Three days later the two areas treated locally with Ledercort and vitamin A had completely cleared.

All the lesions on the patient's left side were then treated with the cream containing Ledercort and vitamin A and all the lesions on the right side were treated with the same concentration of vitamin A in ung. emulsificans aquos. During the next six days both sides improved considerably. The left side, treated with the mixture, was better than the right treated with vitamin A alone. The internal dose of Ledercort was kept constant at 4 mg. b.d. throughout this period.

SUMMARY.

The results obtained from animal experiments with parenteral Ledercort and local vitamin A indicated that psoriasis would be improved by the local application of vitamin A provided that systemic Ledercort was first used to control epidermal activity. This conclusion has been confirmed in a clinical trial on a single patient with psoriasis.

Further clinical investigations with these two substances are being undertaken. A full report of our histochemical findings in psoriatic patients treated with systemic Ledercort, and of our animal experiments together with extended clinical trials will be published later.

We are most grateful to Mrs. J. A. Hardy for her help with the histochemical techniques. We also thank Dr. J. R. Wilson, Medical Director of Lederle, for a generous supply of Ledercort ointment, cream and suspension for clinical trials and animal experiments. The water solubilized vitamin A (aquasol vitamin A) was obtained from U.S. Vitamin Corporation Arlington-Funk Labs., New York, N.Y. R. I. Spearman holds a personal grant from the Medical Research Council.

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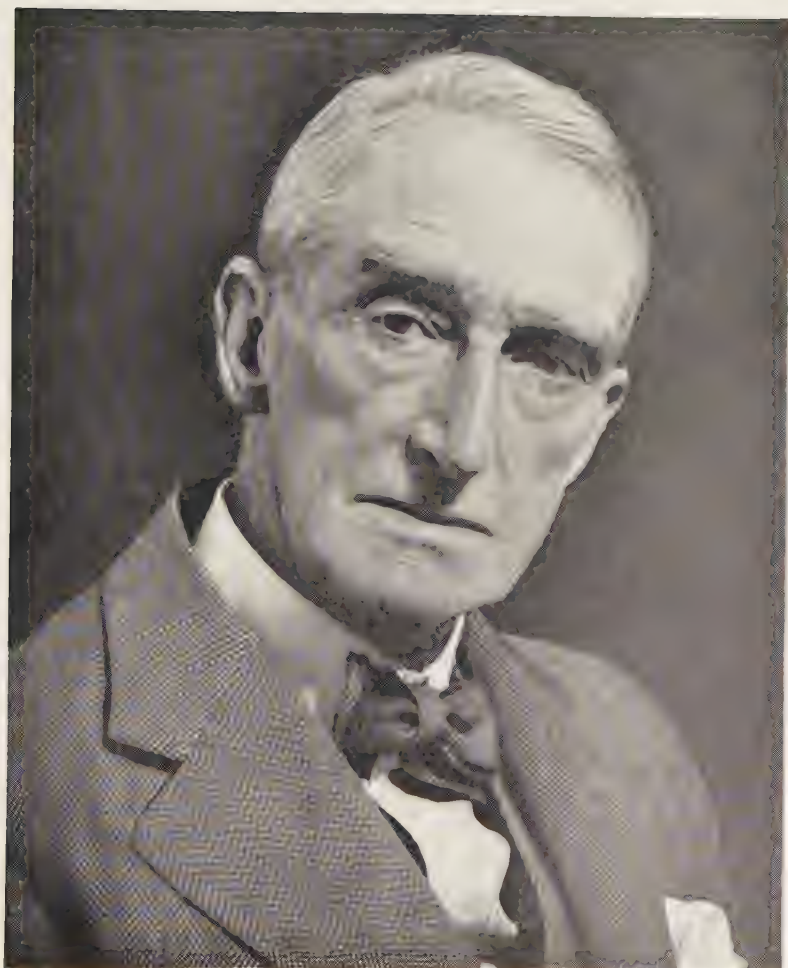
OBITUARY.

DR. W. HERBERT BROWN.

WE record with deep regret the death of William Herbert Brown on 29 March, the day after his 81st birthday.

Born in Glasgow, he was educated at the High School and University of that city, graduated M.B., Ch.B. in 1901, and M.D., with Honours, in 1906. In 1938 he was elected a Fellow of the Royal Faculty of Physicians and Surgeons. In his early days he did some work in Pathology, and also for several years as a general practitioner, but was soon attracted to Dermatology, and became successively Assistant, Chief and finally Consulting Physician for Diseases of the Skin at the Victoria Infirmary. In the first world war he served in the R.A.M.C., mainly in his own specialty and in Venereology. This latter experience he turned to good account when in 1920 he published, jointly with C. F. White, his "Atlas of the Primary and Cutaneous Lesions of Acquired Syphilis in the Male". He was a fine exponent of black-and-white clinical photography, and this Atlas, with its stereoscopic plates, was probably the best thing of its kind at that date. On his return to Glasgow he soon established a high reputation as a teacher, and built a large consulting practice. To a high degree of professional skill he added all the force of a most lovable personality, and many medical colleagues were among his clients. He was not a voluminous writer, but contributed a number of papers to this Journal. He maintained his interest in V.D. for some years, and made the Broomielaw Clinic famous throughout the Seven Seas. An Original Member of the B.A.D., he was its President in 1941, and latterly an Honorary Member. His tall, dignified figure and strong, aquiline features made him conspicuous in any gathering, and he will be sadly missed, particularly from the North British Dermatological Society, of which also he was a founding member.

J. F. S.



CURRENT LITERATURE.

A CONTRIBUTION TO THE STUDY OF EPIDERMOLYSIS BULLOSA OF THE NEWBORN.P. CAREDDU and M. P. BONANNI. (1958) *Giorn. ital. Derm.*, **99**, 306.

A girl, born without skin on the legs, later blistered on the genitals, in the mouth and on the skin of the head, limbs and trunk. Oral steroid therapy partially suppressed the blistering and cessation of treatment was followed by phagedenic ulceration. The skin defect on the legs had shown no signs of healing up to the time of her death at 6 weeks. The blisters were sub-epidermal: the skin defect was an absence of epidermis and follicles, but not sweat glands. "Normal" skin taken at necropsy was microscopically blistered though Nikolsky's sign during life had been absent. Her mother and father had a minor blistering tendency; her elder sister died aged 1 week from the same disease but a half-sister by her mother's earlier marriage with a healthy man was alive and free of skin disease.

The authors found a deficiency of mast cells and condensation of P.A.S. positive material in relation to bullae. They postulate an adrenal cortical deficiency and a local scarcity of mast cells and hence ground substance as the basic cause of this disease.

A. L.

ON A SPECIFIC CYTOLOGICAL FEATURE OF THE BLISTER FLUID IN A CASE OF ECTODERMOSIS EROSIVA PLURIORIFICIALIS.L. MARTINETTI and L. MAZZA. (1958) *Giorn. ital. Derm.*, **99**, 331.

A woman aged 64. Her blister fluid contained histiocyte-like cells many of them in mitosis. They contained granules which were P.A.S. positive (eliminated by diastase) and stained inconsistently with Sudan Black B. These peculiar cells were absent from peripheral blood and sternal marrow. Unfortunately further investigation was impossible because her relations took her home to die.

A. L.

PARALLERGY IN JENNERIAN VACCINATION.F. NARDUCCI. (1958) *Arch. ital. Derm. Sif.*, **29**, 81.

Briefest clinical description of 2 adults in whom vaccination provoked cutaneous hypersensitivity to a substance previously well tolerated. The previous vaccination history is not given. Lengthy discussion on parallergy and metallergy—most obscure.

A. L.

PLETHYSMOGRAPHIC OBSERVATIONS UNDER BASAL CONDITIONS IN ACROCYANOSIS AND IN SOME ACROPATHIES HAVING A CYANOTIC BACKGROUND.L. RASPONTI and L. GIGLI. (1958) *Arch. ital. Derm. Sif.*, **29**, 93.

In acrocyanosis the circulation is reduced, the micropulse is low, slow and rounded. In the late stage of erythema induratum the circulation is reduced but in its early stage and in erythema nodosum the circulation is augmented.

A. L.

A CASE OF MULTIPLE AND MULTIFORM BASAL-CELL TUMOUR.F. NARDUCCI. *Arch. ital. Derm. Sif.*, **29**, 105.

Multiple seborrhoeic warts of the trunk of a woman aged 54. In addition there were basal-cell tumours some atrophic, some crusted, some erythematous, some pigmented, some exuberant. The histology varied accordingly. The previous ingestion of arsenic has not been considered.

A. L.

ADVANCES IN THE TREATMENT OF SKIN DISEASES.G. Hodgson. (1958) *Practitioner*, **181**, 410.

Sedatives help patients with emotional sweating, and cholinergic sweating is reduced or abolished by atropine or anticholinergic drugs. The side effects and contra-indications of these drugs are discussed, as well as their use in cheilopompholyx and miliarial eruptions.

Topical hydrocortisone is not recommended for widespread eczema or chronic cases which probably respond as well to tar preparations. The best results appear in contact dermatitis.

It is sometimes justified to combine an antibiotic to control secondary infection. With systemic steroid therapy the death rate in pemphigus has been reduced from 90% to 33%.

R. J. C.

SOME NEW TREATMENTS FOR PSORIASIS. E. LIPMAN COHEN. (1958) *Practitioner*, **181**, 618.

Nearly half of an unspecified number of patients cleared completely within three weeks on treatment with cyanocobalamin, 1000 μ g. daily intramuscularly. Glycyrrhetic acid in the form of "tar biosone GA" ointment was used in twenty-one psoriatics. Those with pruritus were particularly helped and four of the twenty-one cleared completely, three clearing in less than a month. A single case was treated with aminopterin 0.5 mg. daily for twelve days. There was obvious improvement, but prompt relapse when treatment was stopped. Aminopterin is considered to be a dangerous drug and should never be used for treating psoriasis, except where facilities are available for checking the blood on alternate days.

R. J. C.

OTITIS EXTERNA IN THE TROPICS. R. AKROYD. (1958) *Practitioner*, **181**, 603.

Pseudomonas and other gram-negative organisms are frequently found on culture, whereas in temperate climates gram-positive cocci usually predominate. 125 cases were investigated and it was found that 40% developed otitis externa within three months of residing in the tropics. It appeared that swimming was a contributory factor. There was a satisfactory response to treatment in about three-quarters of the acute cases which were treated either with neomycin-hydrocortisone ointment or chloramphenicol drops.

R. J. C.

ANAPHYLAXIS AFTER ORAL SULPHADIAZINE. P. M. BINNS. (1958) *Lancet*, **i**, 194.

A patient treated four months previously with sulphadiazine reacted to a subsequent dose of this drug by developing widespread urticaria and erythema together with profuse sweating. She omitted the drug for twenty-four hours and then took the tablets regularly for three days without ill effect. A few days later she took a further dose of sulphadiazine and within thirty minutes developed a similar reaction but on this occasion she lost consciousness and became shocked and pulseless. She recovered after injection of adrenaline.

R. H. M.

DERMATITIS CAUSED BY PENICILLIN IN MILK. H. R. VICKERS, L. BAGRATUNI, S. ALEXANDER. (1958) *Lancet*, **i**, 351.

Two patients who developed widespread eczema were found by patch tests to be allergic to penicillin and their history supported the view that their skin eruptions had been provoked by penicillin in milk that they drank daily. Penicillin (4 units per ml.) was found in milk taken by one of the patients. The authors state "If patients previously sensitized to penicillin by local application drink milk containing penicillin, dermatitis may develop and persist indefinitely if its true nature is not recognized".

R. H. M.

THE NATURAL HISTORY OF MALIGNANT GRANULOMA OF THE NOSE. M. M. SINGH, J. F. STOKES, R. A. B. DRURY and J. M. WALSH. (1958) *Lancet*, **i**, 401.

Four fatal cases of malignant granuloma of the nose are described. They all showed evidence of systemic involvement and three had albuminuria and terminal azotaemia. One patient had the complete syndrome of Wegener's granulomatosis—a necrotizing granuloma of the respiratory tract, generalized vasculitis and glomerulonephritis.

The authors suggest that their cases form an arc extending from the local lesions of malignant granuloma of the nose to the full recognizable picture of Wegener's granulomatosis. They comment that the disorder consistently showed three stages.

- (1) A minor rhinological lesion commonly followed by operation.
- (2) The development of a local destructive granuloma.
- (3) The late appearance of systemic lesions.

Suggested treatment is a combination of local radiotherapy and systemic cortico-steroid therapy.

R. H. M.

ADULT SCURVY. R. H. CUTFORTH. (1958) *Lancet*, **i**, 454.

Eleven adults with scurvy are described. Only one showed swollen and bleeding gums, but seven were edentulous. Symptoms were pain, lethargy, anorexia and mental depression, and the chief signs were small bruises on the limbs, extravasation of blood into the tissues and anaemia. Symptoms and signs, including anaemia, responded rapidly to ascorbic acid.

The cases fell into three groups: elderly men living alone; those dieting for medical reasons; and the "food crank".

R. H. M.

THE MECHANISMS OF TRIGLYCERIDE THERAPY IN DERMATOMYCOSES. B. G. KNIGHT. (1957) *J. invest. Derm.*, **28**, 363.

Free fatty acids have better fungistatic properties than their salts. Esterase, produced by fungi, liberates acetic acid from triacetin until, at pH 4 or thereabouts, inhibition takes place. Esterase is of course also present in epidermal cells and in serum. J. H. T. D.

THE USE OF A CYCLOHEXIMIDE-CHLORAMPHENICOL MEDIUM IN ROUTINE CULTURE FOR FUNGI. S. A. ROSENTHAL and D. FURNARI. (1957) *J. invest. Derm.*, **28**, 367.

Among pathogens only *Cryptococcus neoformans*, *Allescheria Boydii*, and *Aspergillus fumigatus* are inhibited by cycloheximide. Sabouraud containing 100 mg. cycloheximide and 50 mg. of chloramphenicol per litre gives 100% better results than plain Sabouraud medium. That this is not wholly due to the suppression of unwanted microbes is shown by the fact that in no less than 26 instances the plain Sabouraud slope remained sterile while the corresponding medicated one grew dermatophytes. It has even been suggested that antibiotics facilitate the change from the parasitic to the saprophytic phase by acting on enzyme systems. (Since we do not completely understand the operation of "green fingers" the authors should have stated what steps were taken to make the media indistinguishable to the investigator.) J. H. T. D.

A SEMI-IN VIVO PROCEDURE FOR TESTING ANTIFUNGAL AGENTS FOR TOPICAL USE.

M. M. DOLAN, J. S. EBELHARE, A. M. KLIGMAN and R. C. BARD. (1957) *J. invest. Derm.*, **28**, 359.

Scrapings from a suitable lesion are placed in a sort of miniature tea-infuser and examined after varying periods of immersion in the fungicide to be tested. J. H. T. D.

ELECTRON MICROSCOPIC STUDY OF KERATOHYALIN IN THE FORMATION OF KERATIN.

E. L. LADEN, P. GETHNER and J. O. ERICKSON. (1957) *J. invest. Derm.*, **28**, 325.

Certain similarities of shape and arrangement of the keratohyalin granules with those of adjacent keratin fibres seem to support the view that the former are direct precursors of the latter. J. H. T. D.

A STUDY OF PHOTOSENSITIVITY OCCURRING WITH CHLORPROMAZINE THERAPY.

J. H. EPSTEIN, L. A. BRUNSTING, M. C. PETERSEN and B. E. SCHWARZ. (1957) *J. invest. Derm.*, **28**, 329.

Of the very large numbers of people who habitually consume chlorpromazine a few develop abnormal reactions to summer sunlight. A 1% solution of the drug completely absorbs wavelengths between 2000 and 3700 Å, and it is thought that the active wavelengths lie between 2967 and 3025 Å. The skin of 9 out of 72 patients developed a reaction, interpreted as an exaggeration of the normal sunburn response, when exposed to a carbon arc lamp. Three of these also had urticarial papular rashes, perhaps a little more intense on exposed parts, as did 4 of the patients who failed to react specifically to light.

Although a very little coproporphyrin was found in the urine of 19 of the patients it was not possible to associate the circumstance with this reaction for which the chemical relationship of chlorpromazine with phenegan, and more remotely with methylene blue, seems to indicate a possible explanation. J. H. T. D.

THE PERSISTENCE OF ALLERGIC ECZEMATOUS SENSITIVITY AND THE CROSS-SENSITIVITY PATTERN TO PARAPHENYLENEDIAMINE. A. A. FISHER, A. PELZIG and N. B. KANOF. (1958) *J. invest. Derm.*, **30**, 9.

Forty-six of fifty patients having given positive patch tests with paraphenylenediamine retained their sensitivity over a period of 3-10 years. Eleven of them reacted also to benzocaine, four to procaine and benzocaine, three to PABA and benzocaine and one to sulphanilimide.

Repeated exposure to paraphenylenediamine neither altered the level of sensitivity nor broadened the established spectrum of cross-sensitivity.

Similar results with patients allergic to nickel and ragweed; but chrome sensitivity appears to be less persistent. J. H. T. D.

THE EFFECT OF PH AND THE PRESENCE OF OTHER ELEMENTS IN SOLUTION ON THE ABSORPTION OF BORON. H. C. FREIMUTH and R. S. FISHER. (1958) *J. invest. Derm.*, 30, 83.

If the clipped body of a rabbit is enveloped in a wet dressing of boric acid or borax there results an appreciable increase in blood boron. The addition of an alkaline buffer inhibits absorption. The urine of rabbits contains about 10 micrograms boron per cc. anyhow, for it is a common constituent of agricultural fertilizers.

J. H. T. D.

BLOOD BORON LEVELS IN HUMAN INFANTS. R. S. FISHER and H. C. FREIMUTH. (1958) *J. invest. Derm.*, 30, 85.

The blood boron was estimated of 71 small children with skin diseases some of whom had received local treatment with boric acid and others has derived their supplies solely from dietary sources, for example currants and oranges. There was little difference between the two groups at a general level of 0.25 γ per ml. Two children who drank some boric lotion in mistake for water had 3.5 γ /ml. (above the lethal level according to Ducey and Williams) and appeared none the worse for it. In the authors' experience of fatal cases the level has been 25 to 50 γ /ml.

J. H. T. D.

STUDIES OF THE MECHANISM OF ALLERGIC ECZEMATOUS CONTACT DERMATITIS. I. FINDINGS ON HUMAN SKIN WITH RADIOACTIVE BICHLORIDE OF MERCURY. V. H. WITTEN, L. D. GRAYSON and V. H. BIRNBAUM. (1957) *J. invest. Derm.*, 28, 339.

An attempt to display the localization and routes of penetration in the skin, normal or known to be sensitized, by means of autoradiography.

J. H. T. D.

THE USE OF A PRECIPITIN TEST TO DIFFERENTIATE CANDIDA ALBICANS FROM CANDIDA STELLATOIDEA. J. R. TRIMBLE. (1957) *J. invest. Derm.*, 28, 349.

Candida albicans is ordinarily distinguished from the others by its sugar reactions and by chlamydospore formation in corn meal agar. This test, using specific rabbit antiserum and an antigen which takes 5 weeks to prepare from the culture, is said to be comparatively expeditious and closely to approximate in accuracy the rabbit pathogenicity test. It will not however distinguish *albicans* from *tropicalis*.

J. H. T. D.

SPECTROPHOTOMETRIC AND ELECTROPHORETIC PATTERNS OF SERA OF PATIENTS WITH POLYMORPHOUS LIGHT ERUPTION. M. M. CAHN, E. J. LEVY, J. M. VANDENBELT and B. SHAFFER. (1958) *J. invest. Derm.*, 31, 93.

There were no characteristic changes in U.V. and visible light absorption spectra or in the electrophoretic patterns of sera of patients with polymorphous light eruption whether in active or quiescent phase or after suppression with mepacrin.

J. H. T. D.

STUDIES ON SILICON IN TISSUES WITH SPECIAL REFERENCE TO SKIN. S. FREGERT. (1958) *J. invest. Derm.*, 31, 95.

While internal organs contain 18–56 γ SiO₂ per gm., epidermis contains 106, hair 90, feathers 340, and the scales in ichthyosis up to nearly 600. Silicon is mostly situated in the alkali-insoluble residue.

J. H. T. D.

SENSITIZING COMPONENT IN THIOSALICYLIC ACID. L. E. GAUL. (1958) *J. invest. Derm.*, 31, 91.

Merthiolate is a very common cause of contact dermatitis. The author has traced its allergenic property to thiophenol. 0.1% in alcohol is the correct concentration for patch testing.

J. H. T. D.

RING CLOSURE AND FUNGISTATIC ACTIVITY. A. A. RENZI, A. C. GARNER and A. BURGER. (1958) *J. invest. Derm.*, 30, 87.

Phenothiazines have a basic structure of 3 benzene rings and most of the work on their fungistatic properties has been concentrated on fiddling about with the side chain. Here are studied the effects of opening the middle ring at position 10. This neither enhances nor diminishes potency, but when a chlorine atom or two are added the improvement is greater than with a closed ring compound.

J. H. T. D.

TOPICAL APPLICATION OF CHLORPROMAZINE: ITS EFFECT ON THE ERYTHEMA RESPONSE TO ULTRAVIOLET LIGHT. J. H. EPSTEIN and L. A. BRUNSTING. (1958) *J. invest. Derm.*, 30, 91.

If you ingest chlorpromazine you may become light sensitive but locally it makes a good sunscreen. J. H. T. D.

THE GERMINATION OF THE FUSEAUX OF MICROSPORUM FULVUM. C. E. WHEELER, W. HARVEY CABANISS and E. P. CAWLEY. (1958) *J. invest. Derm.*, 30, 27.

This is a description of what happens when fuseaux, obtained by lightly brushing the powdery surface of a colony of *M. fulvum*, are incubated on Sabouraud's glucose agar. J. H. T. D.

ISOCITRIC DEHYDROGENASE ACTIVITY OF HUMAN EPIDERMIS. C. N. D. CRUICKSHANK, F. B. HERSHEY and C. LEWIS. (1958) *J. invest. Derm.*, 30, 33.

A beautiful experiment, demonstrating the isocitric dehydrogenase activity of homogenates of skin and of various parts of the epidermis separately, strongly suggests the tricarboxylic (Krebs') cycle does indeed operate in the skin, as in most other mammalian tissues, and that the presence of manganese is essential to it. J. H. T. D.

INDUCTION OF ALLERGIC CONTACT DERMATITIS IN PATIENTS WITH THE LYMPHOMA-LEUKAEMIA COMPLEX. W. L. EPSTEIN. (1958) *J. invest. Derm.*, 30, 39.

Twenty-seven such patients, neither cachectic nor bedfast all showed a significantly reduced sensitizability with 2, 4-dinitrochlorobenzene. J. H. T. D.

INHIBITORS OF LIPEMIA CLEARING IN TISSUES. E. KLEIN, W. F. LEVER and L. L. FEKETE. (1958) *J. invest. Derm.*, 30, 41.

Spleen, kidney and liver and to a rather less extent testis lung and muscle, but in some degree almost all tissues, contain this inhibitor. J. H. T. D.

THE RESPONSE OF THE HUMAN EPIDERMIS TO THE APPLICATION OF CARCINOGENIC HYDROCARBONS. M. G. WILLIAMS. (1958) *J. invest. Derm.*, 30, 13.

Painting 3-methylcholanthrene on intact and Scotch tape-stripped skin failed to produce changes appreciable by the mitosis-counting method here described.

The whole subject of chemical carcinogens is discussed in this attractive and well documented paper. J. H. T. D.

PROTEOLYTIC ACTIVITY IN DERMATOSES: STUDIES OF BLOOD OF PATIENTS WITH PRURITUS. F. E. CORMIA, J. W. DOUGHERTY and SHIRLEY UNRAU. (1958) *J. invest. Derm.*, 30, 21.

A comparison of the levels of plasma protease activator, fibrinolysin and serum protease inhibitor in normal subjects and in patients with severe widespread pruritus attributed to various causes, e.g. Hodgkin's disease, jaundice, diffuse neurodermatitis and disturbances of the psyche, did not reveal significant differences. Scattered itching produced by intradermal injection of trypsin does not appear to be due to activation of profibrinolysis and, in three cases of general pruritus not made worse by trypsin, the serum fibrinolysin inhibitor was not increased.

J. H. T. D.

RINGWORM EPIZOOTICS IN LABORATORY MICE AND RATS: EXPERIMENTAL AND ACCIDENTAL TRANSMISSION OF INFECTION. M. M. DOLAN, A. M. KLIGMAN, P. G. KOBYLINSKI and M. A. MOTSAVAGE. (1958) *J. invest. Derm.*, 30, 23.

Following outbreaks of ringworm among laboratory workers, *T. mentagrophytes* was cultivated from hair plucked from apparently normal laboratory rats and mice in 6 out of 8 consignments from different breeders in percentages varying from 3-66. J. H. T. D.